Ø 003/019

Attorney Docket No.: 5686.200-US

Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

# Amendments To The Claims

The listing of claims will replace all prior versions, and listings, of the claims in the application.

## Listing Of Claims:

Claim 1 (Currently amended) A compound of formula (I):

wherein

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> independently are hydrogen, halogen, -CF<sub>3</sub> or -NO<sub>2</sub>, X and V are =N-,

L is -SO<sub>2</sub>-CH<sub>2</sub>-, -S , -SH<sub>1</sub>-NH<sub>2</sub> or -NH<sub>3</sub>,

M is -NR<sup>9</sup>-CH<sub>2</sub>, -SO<sub>2</sub>-alkylene, -S-alkylene, -SO-alkylene, -NH-, -NH<sub>2</sub> or a valence bond,

wherein R9 is hydrogen, lower alkyl, cycloalkyl or a heteroaryl which is a 3 to 10 membered ring containing one or more heteroatoms selected from nitrogen, oxygen and sulfur,

in which the cycloalkyl and heteroaryl rings may optionally be substituted with one or more substituents independently selected from halogen, lower alkyl, lower alkanoyl, -OH, -CH2OH, -NO2, -CN, -C(O)OH, -O-lower alkyl, -C(O)OCH3, -C(O)NH2, -OCH<sub>2</sub>C(O)NH<sub>2</sub>, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, -OCHF<sub>2</sub>, -CF<sub>3</sub> and -OCF<sub>3</sub>,

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

A and B independently are hydrogen or lower alkyl,

as well as any optical or geometric isomer or mixture of optical or geometric isomers, or any tautomeric form thereof or a pharmaceutically acceptable salt thereof.

Claims 2-36 (Cancelled)

Claim 37 (Currently Amended) A compound of claim-1 of formula (V):

wherein

L is -SO<sub>2</sub>-CH<sub>2</sub>-, -S-, or -SH,

M is -NR9-CH2, -SO2-alkylene, -S-alkylene, -SO-alkylene, -NH-, -NH2 or a valence bond,

wherein R<sup>9</sup> is hydrogen, lower alkyl, cycloalkyl or a heteroaryl which is a 3 to 10 membered ring containing one or more heteroatoms selected from nitrogen, oxygen and sulfur,

in which the cycloalkyl and heteroaryl rings may optionally be substituted with one or more substituents independently selected from halogen, lower alkyl, lower alkanoyl, -OH, -CH2OH, -NO2, -CN, -C(O)OH, -O-lower alkyl, -C(O)OCH3, -C(O)NH2, -OCH<sub>2</sub>C(O)NH<sub>2</sub>, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, -OCHF<sub>2</sub>, -CF<sub>3</sub> and -OCF<sub>3</sub>,

A and B independently are hydrogen or lower alkyl,

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

as well as any optical or geometric isomer or mixture of optical or geometric isomers, or any tautomeric form thereof or a pharmaceutically acceptable salt thereof.

Claims 38-51 (Cancelled)

Claim 52 (Previously presented) A pharmaceutical composition comprising a compound according to claim 1 together with a pharmaceutically acceptable carrier or excipient.

Claim 53 (Previously presented) A pharmaceutical composition according to claim 52 in unit dosage form, said composition comprising from about 0.05 mg to about 1000 mg of the compound.

Claims 54-64 (Cancelled)

Claim 65 (Currently amended) A method for the treatment of disorders or diseases wherein an activation of the human GLP-1 receptor is beneficial, said method comprising administering to a subject in need thereof an effective amount of a compound according to elaim-1 of formula (I):

wherein

 $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  independently are hydrogen, halogen, -CF<sub>1</sub> or -NO<sub>2</sub>, X and V are =N-,

Attorney Docket No.: 5686.200-US

Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Piled: January 14, 2000 Inventors: Teng et al.

L is -SO2-CH2-, -S-, -SH, -NH2 OT -NH-,

M is -NR9-CH2, -SO2-alkylene, -S-alkylene, -SO-alkylene, -NH-, -NH2 or a valence bond,

wherein R<sup>9</sup> is hydrogen, lower alkyl, cycloalkyl or a heteroaryl which is a 3 to 10 membered ring containing one or more heteroatoms selected from nitrogen, oxygen and sulfur, in which the cycloalkyl and heteroaryl rings may optionally be substituted with one or more substituents independently selected from halogen, lower alkyl, lower alkanoyl,

-OH, -CH<sub>2</sub>OH, -NO<sub>2</sub>, -CN, -C(O)OH, -O-lower alkyl, -C(O)OCH<sub>3</sub>, -C(O)NH<sub>2</sub>, 
OCH<sub>7</sub>C(O)NH<sub>2</sub>, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, -OCHF<sub>2</sub>, -CF<sub>3</sub> and -OCF<sub>3</sub>.

A and B independently are hydrogen or lower alkyl,

as well as any optical or geometric isomer or mixture of optical or geometric isomers, or any tautomeric form thereof or a pharmaceutically acceptable salt thereof.

Claim 66 (Previously presented) The method according to claim 65 wherein the effective amount of the compound is in the range of from about 0.05 mg to about 2000 mg per day.

Claim 67 (Previously presented) A pharmaceutical composition according to claim 52 in unit dosage form, said composition comprising from about 0.1 mg to about 500 mg of the compound.

Claim 68 (Previously presented) A pharmaceutical composition according to claim 52 in unit dosage form, said composition comprising from about 0.5 mg to about 200 mg of the compound.

Attorney Docket No.: 5686.200-US

Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

Claim 69 (Previously presented) The method according to claim 65 wherein the effective amount of the compound is in the range of from about 0.1 mg to about 1000 mg per day.

Claim 70 (Previously presented) The method according to claim 65 wherein the effective amount of the compound is in the range of from about 0.5 mg to about 500 mg per day.

Claim 71 (New) A pharmaceutical composition comprising a compound according to claim 37 together with a pharmaceutically acceptable carrier or excipient.

Claim 72 (New) A pharmaceutical composition according to claim 71 in unit dosage form, said composition comprising from about 0.05 mg to about 1000 mg of the compound.

Claim 73 (New) A pharmaceutical composition according to claim 71 in unit dosage form, said composition comprising from about 0.1 mg to about 500 mg of the compound.

Claim 74 (New) A pharmaceutical composition according to claim 71 in unit dosage form, said composition comprising from about 0.5 mg to about 200 mg of the compound.

Claim 75 (New) A method for the treatment of disorders or diseases wherein an activation of the human GLP-1 receptor is beneficial, said method comprising administering to a subject in need thereof an effective amount of a compound of formula (V):

wherein

Ø 008/019

Attorney Docket No.: 5686.200-US Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

L is -SO<sub>2</sub>-CH<sub>2</sub>-, -S-, -SH, -NH<sub>2</sub> or -NH-,

M is -NR9-CH2, -SO2-alkylene, -S-alkylene, -SO-alkylene, -NH-, -NH2 or a valence bond,

wherein R<sup>o</sup> is hydrogen, lower alkyl, cycloalkyl or a heteroaryl which is a 3 to 10 membered ring containing one or more heteroatoms selected from mitrogen, oxygen and sulfur,

in which the cycloalkyl and heteroaryl rings may optionally be substituted with one or more substituents independently selected from halogen, lower alkyl, lower alkanoyl, -OH, -CH2OH, -NO2, -CN, -C(O)OH, -O-lower alkyl, -C(O)OCH3, -C(O)NH2, -OCH<sub>2</sub>C(O)NH<sub>2</sub>, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -SO<sub>2</sub>NH<sub>2</sub>, -OCHF<sub>2</sub>, -CF<sub>3</sub> and -OCF<sub>3</sub>,

A and B independently are hydrogen or lower alkyl,

as well as any optical or geometric isomer or mixture of optical or geometric isomers, or any tautomeric form thereof or a pharmaceutically acceptable salt thereof.

Claim 76 (New) The method according to claim 75 wherein the effective amount of the compound is in the range of from about 0.05 mg to about 2000 mg per day.

Claim 77 (New) The method according to claim 75 wherein the effective amount of the compound is in the range of from about 0.1 mg to about 1000 mg per day.

Claim 78 (New) The method according to claim 75 wherein the effective amount of the compound is in the range of from about 0.5 mg to about 500 mg per day.

Claim 79 (New) A compound selected from the group consisting of 6,7-Dichloro-3-methyl-2-(methylsulfonyl)quinoxaline, (6,7-Dichloro-3-methylsulfonylquinoxalin-2-yl)amine,

**図** 009/019

Attorney Docket No.: 5686.200-US

Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

- 6,7-Dichloro-2-methylsulfonyl-3-(methylsulfonyl)methyl-quinoxaline,
- 6,7-Dichloro-2-isopropyl-3-(isopropyl-2-sulfonyl)quinoxaline,
- 6,7-Dichloro-2-isopropyl-3-(methylsulfonyl)quinoxaline,
- 6,7-Dichloro-2-(isopropylsulfonyl)-3-[(isopropylsulfonyl)methyl]quinoxaline,
- 6,7-Dichloro-2-isobutyl-3-(methylsulfonyl)quinoxaline,
- 2-(Sec-butyl)-6,7-dichloro-3-(methylsulfonyl)quinoxaline,
- N-[6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl]-N-isopropylamine,
- N-(6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl)-N-methyl-N-isopropylamine,
- N-{6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl}-N-ethylamine,
- N-(6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl]-N,N-dimethylamine,
- 6.7-Dichloro-3-ethyl-2-(methylsulfonyl)quinoxaline,
- 6.7-Dichloro-2-(methylsulfonyl)-3-hexylquinoxaline,
- 6,7-Dichloro-2-(methylsulfonyl)-3-propylquinoxaline,
- 6,7-Dichloro-2-(isopropylsulfonyl)-3-propylquinoxaline,
- N-[6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl]-N-tert-butylamine,
- N-[6,7-Dichloro-3-(methylsulfonyl)-2-quinoxalinyl]-N-isobutylamine,
- 5,6,7,8-Tetrachloro-2-isopropyl-3-(methylsulfonyl)quinoxaline,

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

- (6,7-Dichloro-3-methylsulfonylquinoxalin-2-yl)cyclopropylamine,
- (6,7-Dichloro-3-methylsulfonylquinoxalin-2-yl)cyclopentylamine,
- (6,7-Dichloro-3-methylsulfonylquinoxalin-2-yl)-sec-butylamine,
- (6,7-Dichloro-)-3-(methylsulfonyl)quinoxalin-2-yl)-1-ethylpropylamine,
- (7-Chloro-3-(methylsulfonyl)-6-nitroquinoxalin-2-yl)sec-butylamine,
- (6-Chloro-3-methylsulfonyl-7-nitro-8-trifluoromethylquinoxalin-2-yl)isopropylamine,
- (6,7-Dichloro-3-(methylsulfonyl)-quinoxalin-2-yl)tert-pentylamine,
- 6,7-Dichloro-2-(isopropylsulfanyl)-3-(methylsulfonyl)quinoxaline,
- (5-Chloro-3-methylsulfonyl-7-trifluoromethyl-2-quinoxalin-2-yl)-tert-butylamine,
- (3-Methylsulfonyl-6,7-dinitroquinoxalin-2-yl)-tert-butylamine,
- 6-Chloro-2-(3-methylbutylsulfonyl)quinoxaline,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(2,4-dichlorophenyl)ethyl]amine,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(2-fluorophenyl)ethyl]amine,
- 3-[2-(6,7-Dichloro-3-methanesulfonyl-quinoxalin-2-ylamino)ethyl]phenol,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(3-fluorophenyl)ethyl]amine,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)dimethylamine,
- 6,7-Dichloro-2-isopropylsulfanyl-3-methanesulfonylquinoxaline,
- (6-Chloro-3-methanesulfonylquinoxalin-2-yl)dimethylamine,
- 6-Chloro-3-isopropylsulfanyl-2-methanesulfonylquinoxaline,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(2,4-dichlorophenyl)ethyl]amine,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(2-fluorophenyl)ethyl]amine,
- 3-[2-(6,7-Dichloro-3-methanesulfonyl-quinoxalin-2-ylamino)ethyl]phenol,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)-[2-(3-fluorophenyl)ethyl]amine,
- (6,7-Dichloro-3-methanesulfonylquinoxalin-2-yl)dimethylamine,
- 6,7-Dichloro-2-isopropylsulfanyl-3-methanesulfonylquinoxaline,
- (6-Chloro-3-methanesulfonylquinoxalin-2-yl)dimethylamine, and
- 6-Chloro-3-isopropylsulfanyl-2-methanesulfonylquinoxaline

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

as well as any optical or geometric isomer or mixture of optical or geometric isomers, or any tautomeric form thereof or a pharmaceutically acceptable salt thereof.

Claim 80 (New) A pharmaceutical composition comprising a compound according to claim 79 together with a pharmaceutically acceptable carrier or excipient.

Claim 81 (New) A pharmaceutical composition according to claim 80 in unit dosage form, said composition comprising from about 0.05 mg to about 1000 mg of the compound.

Claim 82 (New) A pharmaceutical composition according to claim 80 in unit dosage form, said composition comprising from about 0.1 mg to about 500 mg of the compound.

Claim 83 (New) A pharmaceutical composition according to claim 80 in unit dosage form, said composition comprising from about 0.5 mg to about 200 mg of the compound.

Claim 84 (New) A method for the treatment of disorders or diseases wherein an activation of the human GLP-1 receptor is beneficial, said method comprising administering to a subject in need thereof an effective amount of a compound of claim 79.

Claim 85 (New) The method according to claim 84 wherein the effective amount of the compound is in the range of from about 0.05 mg to about 2000 mg per day.

Claim 86 (New) The method according to claim 84 wherein the effective amount of the compound is in the range of from about 0.1 mg to about 1000 mg per day.

Claim 87 (New) The method according to claim 84 wherein the effective amount of the compound is in the range of from about 0.5 mg to about 500 mg per day.

Ø 012/019

Attorney Docket No.: 5686.200-U\$

Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

## Remarks/Arguments

Reconsideration and allowance are respectfully requested. Claims 1, 37, 52-53 and 65-87 are pending and are at issue following entry of this Amendment. Claim 1 has been amended for a second time to clarify the number and nature of the heteroatoms in the R9 heteroaryl moiety and to overcome the cited prior art. Added claims 71-78 depend from previously presented claim 37 and added claims 79-87 are directed to specific compounds from the Examples that fall within the elected invention. The amendments to the claims presented herein therefore do not add new matter and will not require any further search by the Examiner. Accordingly, the Examiner is requested to enter these amendments.

## Rejections under 35 U.S.C. §112 second paragraph

Claims 1, 37, 52-53, and 65-70 are rejected under 35 U.S.C. §112, second paragraph as being indefinite on the following grounds:

> A) over the recitation of R9 (the variable M in claim 1 can be NR9-CH2-) as a heteroaryl because the claims are silent about the number and nature of the heteroatoms in the ring and their exact point of connection with the N of the bridge when present; and

B) claim 65, for not being limited to a single disease or disorder; the Examiner stating that the claim should be limited to the specific diseases as per the tests conducted on page 166 of the specification.

These rejections are respectfully traversed and each rejection is addressed below:

A) claim 1 has been amended to recite the number and nature of the heteroatoms that may be in the heteroaryl ring and Applicants submit that the ring may be connected to the bridging nitrogen at any ring atom that would permit such a connection.

Ø 013/019

Attorney Docket No.: 5686.200-US Express Mail Label No.: EV 246880709 US

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

> B) claim 65 as written has a clear and definite meaning to one of ordinary skill in the art. Under section 112, second paragraph, the breadth of a claim is not to be equated with indefiniteness. Rather, all that is required by section 112, second paragraph is that one of ordinary skill in the art reading the claims would understand the nature of the language recited in the claim in light of the specification. Here, claim 65 is directed to a method for the treatment of disorders or diseases wherein an activation of the human GLP-1 receptor is beneficial and the specification clearly discloses on page 41, lines 6-17 disorders and diseases where activation of the GLP-1 receptor is beneficial. Thus, the language of claim 65 is in compliance with the requirements of section 112, second paragraph and should not be limited to a single disease or disorder.

For the foregoing reasons, Applicants submit that the above amendments and remarks address the rejections of the claims under 35 U.S.C. §112, second paragraph and withdrawal of these rejections is therefore respectfully requested.

## Rejections under 35 U.S.C. §102 (b)

Claims 1, 37, 52-53 and 65-70 are rejected under 102 (b) as being anticipated by Bata et al WO 97/19934, Sam et al US patent No. 4,022,777, Wozniak et al [Indian J. of Heterocyclic Chemistry (1994) 42:75-80] and Kyowa et al JP 55127205 and the Chemical Abstract reference numbers cited on pages 4-5 of the Office Action as attributable to these references. Applicants respectfully traverse this rejection as follows!:

First, it is believed that with respect to claim 1 and claims 52-53 and 67-68 dependent therefrom, the amendment to claim 1 to delete that L can be "-S-, -SH, -NH2 or -NH-", renders this rejection moot.

Application No.: 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

Second, with respect to claim 37 (and claims 71-74 dependent therefrom) where R<sup>1</sup> and R<sup>2</sup> are fixed as hydrogen and R<sup>2</sup> and R<sup>3</sup> are fixed as chlorine, it is believed that the rewriting of this claim as an independent claim where L can be -SO<sub>2</sub>-CH<sub>2</sub>-, -S-, or -SH but not -NH<sub>2</sub> or -NH- renders this rejection moot.

Third, it is believed that no amendment to the compounds used in the methods of claims 65 and 75 (these claims recite the compounds of claims 1 and 37 respectfully as they were written prior to the present Amendment) is necessary since the prior art compounds cited by the Examiner are chemical intermediates and not final products and the four prior art references cited under the 102 rejection do not teach the use of the compounds described therein for the treatment of disorders or diseases wherein an activation of the human GLP-1 receptor is beneficial [WO 97/19934 discloses that its compounds show significant activity at the glycine binding site of the NDMA receptor (page 1, lines 26-270), USP 4,022,777 as useful as fungicides (see col. 1, lines 12-13), JP 55167205 as useful as herbicides; and Wozniak says nothing about the utility of the compounds described therein]. Finally, Applicants submit that claims 79-87, directed to specific examples in the application, are free of the cited art.

<sup>1</sup> Applicants acknowledge the Examiner's reference to the CASRN #s listed on page 2 of the Office Action and while the Examiner has not applied these as part of the formal 102 (b) rejection, Applicants have, in the interests of furthering prosecution, also addressed these CASRN#s in responding to this Office Action

**2**015/019

Attorney Docket No.: 5686.200-US Express Mail Label No.: EV 246880709 US

Application No.; 09/483,504 Filed: January 14, 2000 Inventors: Teng et al.

Accordingly, in view of the above amendments and remarks, withdrawal of this rejection is respectfully requested.

NOVO NORDISK LEGAL

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

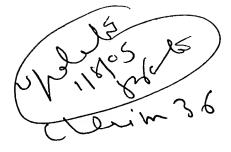
Date: January 5, 2005

Novo Nordisk, Inc. 100 College Road West Princeton, NJ 08540 (609) 987-5800

CUSTOMER NUMBER 23650 PATENT TRADEMARK OFFICE

Gren Rega 609 987 593, Jax 809 9197741

09483504.35 Page 1



Welcome to STN International! Enter x:x

LOGINID:sssptal6llsxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Web Page URLs for STN Seminar Schedule - N. America
NEWS
NEWS
         Apr 08
                 "Ask CAS" for self-help around the clock
NEWS
        Apr 09
                 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS
        Apr 09
                 ZDB will be removed from STN
                 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS
        Apr 19
NEWS
        Apr 22
                 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS
         Apr 22
                 BIOSIS Gene Names now available in TOXCENTER
NEWS
        Apr 22
                 Federal Research in Progress (FEDRIP) now available
NEWS
         Jun 03
                 New e-mail delivery for search results now available
NEWS 10
         Jun 10
                 MEDLINE Reload
                 PCTFULL has been reloaded
NEWS 11
         Jun 10
NEWS 12
         Jul 02
                 FOREGE no longer contains STANDARDS file segment
NEWS 13
         Jul 22
                 USAN to be reloaded July 28, 2002;
                 saved answer sets no longer valid
NEWS 14
         Jul 29
                 Enhanced polymer searching in REGISTRY
                 NETFIRST to be removed from STN
NEWS 15
        Jul 30
                 CANCERLIT reload
NEWS 16
        Aug 08
NEWS 17
         Aug 08
                 PHARMAMarketLetter (PHARMAML) - new on STN
         Aug 08
NEWS 18
                 NTIS has been reloaded and enhanced
NEWS 19
         Aug 19
                 Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS 20
                 IFIPAT, IFICDB, and IFIUDB have been reloaded
         Aug 19
NEWS 21
                 The MEDLINE file segment of TOXCENTER has been reloaded
        Aug 19
NEWS 22
         Aug 26
                 Sequence searching in REGISTRY enhanced
         Sep 03
NEWS 23
                 JAPIO has been reloaded and enhanced
NEWS 24
         Sep 16
                 Experimental properties added to the REGISTRY file
NEWS 25
         Sep 16
                 CA Section Thesaurus available in CAPLUS and CA
                 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 26
        Oct 01
NEWS 27
        Oct 21
                 EVENTLINE has been reloaded
NEWS 28 Oct 24
                 BEILSTEIN adds new search fields
NEWS 29
        Oct 24
                 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25
                 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18
                 DKILIT has been renamed APOLLIT
NEWS 32 Nov 25
                 More calculated properties added to REGISTRY
NEWS 33 Dec 02
                 TIBKAT will be removed from STN
NEWS 34 Dec 04
                 CSA files on STN
NEWS 35 Dec 17
                 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36 Dec 17
                 TOXCENTER enhanced with additional content
NEWS 37
        Dec 17
                Adis Clinical Trials Insight now available on STN
NEWS 38
        Dec 30
                 ISMEC no longer available
                 NUTRACEUT offering one free connect hour in February 2003
NEWS 39
         Jan 21
NEWS 40
        Jan 21
                 PHARMAML offering one free connect hour in February 2003
NEWS 41
        Jan 29
                 Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
NEWS 42 Feb 13
                 CANCERLIT is no longer being updated
```

Page 2

09483504.35

NEWS WWW

	NEWS	43	Feb	24	METADEX enhancements
	NEWS	44	Feb	24	PCTGEN now available on STN
	NEWS	45	Feb	24	
	NEWS	46	Feb	26	NTIS now allows simultaneous left and right truncation
	NEWS	47	Feb	26	
	NEWS	48	Mar	04	
	NEWS				
					EVENTLINE will be removed from STN
	NEWS	51	Mar	24	PATDPAFULL now available on STN
	NEWS	52	Mar	24	Additional information for trade-named substances without
					structures available in REGISTRY
	NEWS	53	Mar	24	Indexing from 1957 to 1966 added to records in CA/CAPLUS
	NEWS	WS EXPRESS		Ja	nuary 6 CURRENT WINDOWS VERSION IS V6.01a,
		CU	RRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),		
				AN	D CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
	NEWS HOURS		ST	N Operating Hours Plus Help Desk Availability	
	NEWS INTER			Ge	neral Internet Information
	NEWS LOGIN			We	lcome Banner and News Items
	NEWS PHONE			Di	rect Dial and Telecommunication Network Access to STN

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

CAS World Wide Web Site (general information)

FILE 'HOME' ENTERED AT 07:44:25 ON 04 APR 2003

=> file registry
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 07:44:36 ON 04 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 APR 2003 HIGHEST RN 501410-52-2 DICTIONARY FILE UPDATES: 2 APR 2003 HIGHEST RN 501410-52-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Patel <4/4/2003>

Crossover limits have been increased. See HELP CROSSOVER for details.

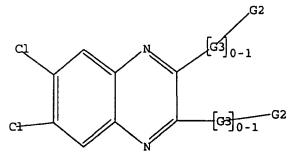
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> Uploading 09483504.7

STRUCTURE UPLOADED Ll

=> d 11

L1 HAS NO ANSWERS Ll STR



G1

G2 C, H, CF3, ON, NO2, Cb

G3 C,S,N,P

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 07:54:22 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -86 TO ITERATE

100.0% PROCESSED 86 ITERATIONS

SEARCH TIME: 00.00.01

19 ANSWERS

FULL FILE PROJECTIONS:

ONLINE \*\*COMPLETE\*\*

\*\*COMPLETE\*\* BATCH

PROJECTED ITERATIONS:

1164 TO 2276

PROJECTED ANSWERS:

119 TO 641

L2

19 SEA SSS SAM L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION FULL ESTIMATED COST

0.40 0.61

FILE 'CAPLUS' ENTERED AT 07:54:29 ON 04 APR 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

Patel

09483504.7 Page 4

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 4 Apr 2003 VOL 138 ISS 15 FILE LAST UPDATED: 3 Apr 2003 (20030403/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> file registry
COST IN U.S. DOLLARS

SINCE FILE TOTAL-ENTRY SESSION 0.42 1.03

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 07:55:14 ON 04 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 APR 2003 HIGHEST RN 501410-52-2 DICTIONARY FILE UPDATES: 2 APR 2003 HIGHEST RN 501410-52-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s 11 sss full FULL SEARCH INITIATED 07:55:30 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 1717 TO ITERATE

100.0% PROCESSED 1717 ITERATIONS SEARCH TIME: 00.00.01

235 ANSWERS

L3 235 SEA SSS FUL L1

Patel

09483504.7 Page 5

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 148.15 149.18

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 07:55:35 ON 04 APR 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 4 Apr 2003 VOL 138 ISS 15 FILE LAST UPDATED: 3 Apr 2003 (20030403/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L4 100 L3

=> d l4 fbib hitstr abs total

- L4 ANSWER 1 OF 100 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:389421 CAPLUS
- DN 137:126416
- TI Synthesis and application of 2-styryl-6,7-dichlorothiazolo[4,5-b] quinoxaline based fluorescent dyes: part 3
- AU Sonawane, N. D.; Rangnekar, D. W.
- CS Dyes research laboratory, Department of Chemical Technology, University of Mumbai, Mumbai, 400 019, India
- SO Journal of Heterocyclic Chemistry (2002), 39(2), 303-308 CODEN: JHTCAD; ISSN: 0022-152X
- PB HeteroCorporation
- DT Journal
- LA English
- OS CASREACT 137:126416
- IT 443795-59-3P, 6,7-Dichloro-2,3-quinoxalinediamine
  RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn., properties and application of styryl dichlorothiazoloquinoxaline fluorescent dyes)

- RN 443795-59-3 CAPLUS
- CN 2(1H)-Quinoxalinethione, 3-amino-6,7-dichloro- (9CI) (CA INDEX NAME)

$$C1 \xrightarrow{N} NH_2$$

IT 55295-04-0, 6,7-Dichloro-2,3-quinoxalinedithiol
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn., properties and application of styryl dichlorothiazologuinoxaline fluorescent dyes)

RN 55295-04-0 CAPLUS

CN 2,3-Quinoxalinedithione, 6,7-dichloro-1,4-dihydro- (9CI) (CA INDEX NAME)

AB A new efficient synthesis of 2-styryl-6,7-dichlorothiazolo[4,5-b]quinoxaline-based fluorescent dyes was achieved by the condensation of 2-methyl-6,7-dichlorothiazolo[4,5-b]quinoxaline with selected 4-(dialkylamino)arylaldehydes and heteroarylaldehydes in the presence of piperidine. The coloristic, fluorophoric, and polyester dyeing properties of these dyes were studied.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 100 CAPLUS COPYRIGHT 2003 ACS

AN 2002:316926 CAPLUS

DN 137:210566

TI Quinoxaline 1,4-dioxides: hypoxia-selective therapeutic agents

AU Diab-Assef, Mona; Haddadin, Makhluf J.; Yared, Pierre; Assaad, Chafika; Gali-Muhtasib, Hala U.

CS Department of Biology, American University of Beirut, Beirut, Lebanon

SO Molecular Carcinogenesis (2002), 33(4), 198-205 CODEN: MOCAE8; ISSN: 0899-1987

PB Wiley-Liss, Inc.

DT Journal

LA English

IT 60680-42-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

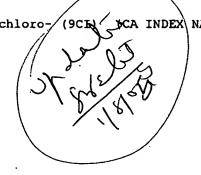
(quinoxaline dioxides as hypoxia-selective antitumor agents)

RN 60680-42-4 CAPLUS

CN Methanone, (6,7-dichloro-1,4-dioxido-3-phenyl-2-quinoxalinyl)phenyl- (9CI) (CA INDEX NAME)

RN 18238-08-9 CAPLUS

CN 2(1H)-Quinoxalinone, 5,6,7,8-tetrachloro-/(9CL) CA INDEX NAME)



RN 18392-45-5 CAPLUS

CN Quinoxaline, 5,6,7,8-tetrachloro-2,3-bis(dichloromethyl)- (8CI) (CA INDEX NAME)

GI For diagram(s), see printed CA Issue.

AB 4,5,6,7-Tetrachlorobenzotriazole and its 1-hydroxy deriv. were reduced with Zn and HCl to give 3,4,5,6-tetrachloro-o-phenylenediamine (I, R = Cl) in good yield. The corresponding diamines (I, R = Me or F) were obtained similarly from 4,5,7-trichloro-6-methyl-(or fluoro)benzotriazole. Alternative syntheses of the tetrachloro- and methyltrichlorophenylenediamines are described. Benzimidazoles, quinoxalines, and other heterocycles derived from the diamines, esp. from tetrachloro-o-phenylenediamine, are reported. 26 references.

L4 ANSWER 243 OF 250 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1967:496531 CAPLUS

DN 67:96531

TI Quinoxalines as analytical reagents. I. Derivatives containing the copper(I)-specific grouping

AU Stephen, William I.; Uden, Peter C.

CS Univ. Birmingham, Birmingham, UK

SO Analytica Chimica Acta (1967), 39(3), 357-68 CODEN: ACACAM; ISSN: 0003-2670

DT Journal

LA English

IT 17401-72-8P 17401-73-9P RL: PREP (Preparation)

(prepn. of)

RN 17401-72-8 CAPLUS

CN Quinoxaline, 6,7-dichloro-2,3-di-2-pyridinyl- (9CI) (CA INDEX NAME)



RN 17401-73-9 CAPLUS

CN Quinoxaline, 6,7-dichloro-2,3-bis(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

AB The prepn., phys. properties, and Cu(I) chelating properties are described of 2,3-bis(2-pyridyl)-quinoxaline (I), 12 derivs. of I prepd. from 2,2'-pyridil[1,2-dioxo-1,2-di(2-pyridyl)ethane]; 2,3-bis[2-(6methylpyridyl)]quinoxaline (II), and 12 derivs. of II prepd. from 6,6'-dimethyl-2,2'-pyridil[1,2-dioxo-1,2-bis-(6-methylpyridyl)ethane] and aromatic or heterocyclic diamines. I and II and the 24 derivs. contain the Cu(I)-specific cuproine grouping: X-C:N-C-C-N:C-X. The max. absorption and molar absorptivities, .epsilon., in EtOH soln., are given of I, II, the 24 analogs of I and II; and of the Cu(I) chelates of the same compds., after extg. into amyl alc. at pH 4.7. To det. 1-100 ppm. Cu2+ with II, add to a 1-ml. aliquot of the Cu2+ soln. 10 ml. of pH 4.7 0.1M NaOAc-0.1M HOAc buffer, 1 ml. of 1% aq. NH2OH.HCl or freshly prepd. 1% ascorbic acid soln., and 4 ml. of 0.1% II (in EtOH). Mix well, and ext. twice with 4-ml. vols. of isoamyl alc., and collect the org. exts. in a flask. Dil. to 10 ml. with isoamyl alc., and measure the absorbance of the soln. at 525 m.mu. vs. isoamylalc. Beer's law holds for 0-100 ppm. of Cu2+ in the final ext. Prep. the absorbanceconcn. calibration graph in the same way with known amts. of Cu2+. The limit of detection is 1:5 .times. 107, approx. the same as that for cuproine. The reaction of Cu2+ with I gives an orange aq. soln. (max. 445 m.mu.) at high Cu2+/I ratios; when the I is increased, the broad max. becomes .apprx.500 m.mu.. Only Ti3+ at pH <2 (max. 608 m.mu. with II) gave a color reaction with the quinoxaline compds. In the given conditions, Ti3+ and Fe2+ in cation/Cu2+ ratios of 100 do not interfere.

L4 ANSWER 244 OF 250 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1965:416869 CAPLUS

DN 63:16869

OREF 63:2973d-g

TI The dimethyl sulfoxide oxidation of 2,3-bis(bromomethyl)quinoxaline

AU Moriconi, Emil J.; Fritsch, Albert J.

09483504.8 Page 1287

CRN 5424-05-5 CMF C8 H7 N3

RN 115747-27-8 CAPLUS

CN 2-Quinoxalinamine, monoperchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 7601-90-3 CMF Cl H O4

CM 2

CRN 5424-05-5 CMF C8 H7 N3

AB Stationary and time-resolved luminescence methods were used to investigate various protonated forms of 2-aminoquinoxaline and 2,3-diaminoquinoxaline. H+ attachment to 2-aminoquinoxaline monocation was discovered in the 1st excited singlet electronic state. Three different protonated structures of 2,3-diaminoquinoxaline were obsd.

L3 ANSWER 639 OF 1398 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1988:473395 CAPLUS

DN 109:73395

TI Dissymmetry of certain substituted dipyridotetraazapentalenes.

AU Pereira, David E.; Clauson, Gary L.; Leonard, Nelson J.

CS Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA

SO Tetrahedron (1987), 43(21), 4931-46

CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA English

OS CASREACT 109:73395

#### 09483504.8 Page 1542

Trujillo, William A. Velsicol Chem. Corp., Chicago, IL, 60611, USA CS Journal of Liquid Chromatography (1980), 3(8), 1219-26 SO CODEN: JLCHD8; ISSN: 0148-3919 DT Journal English LA 59-40-5 IT RL: ANT (Analyte); ANST (Analytical study) (detn. of, in rodenticide concs., by high-performance lig. chromatog.) RN 59-40-5 CAPLUS Benzenesulfonamide, 4-amino-N-2-quinoxalinyl- (9CI) (CA INDEX NAME) CN

GΙ

AB Warfarin (I) [81-81-2] and sulfaquinoxaline [59-40-5] are active ingredients in formulated rodenticide concs. They are solvent-extd.; after injection into a liq. chromatograph, a simple buffered mobile phase is used to elute I as a paired ion and sulfaquinoxaline as an ion-suppressed nonionic species by reverse phase chromatog. A variable wavelength UV detector and an external std. calibration were used for quantitation.

L3 ANSWER 857 OF 1398 CAPLUS COPYRIGHT 2003 ACS on STN

ΑN 1980:568226 CAPLUS

DN 93:168226

ΤI Alkynyl- and dialkylnylquinoxalines. Synthesis of condensed quinoxalines

ΑU

Ames, Donald E.; Brohi, M. Ismail Chem. Dep., Chelsea Coll., London, SW3 6LX, UK CS

I

SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1980), (7), 1384-9 CODEN: JCPRB4; ISSN: 0300-922X

DTJournal

LΑ English

IT 75163-28-9P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and condensation reaction of, with amines)

RN 75163-28-9 CAPLUS